Perioperative cerebral and somatic oxygenation in neonates with hypoplastic left heart syndrome or transposition of the great arteries

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Objective: Significant depression in cerebral oxygen saturation has been observed in patients with hypoplastic left heart syndrome (HLHS) undergoing Norwood operations. We monitored cerebral oxygen saturation with near-infrared spectroscopy before and after this procedure. Patients with transposition of great arteries (TGA) before and after arterial switch operation were also studied to elucidate whether post–cardiopulmonary bypass (CPB) changes in cerebral oxygen saturation are related to CPB or hemodynamic alterations inherent in single-ventricle physiology.

Methods: We monitored 33 patients with HLHS and 20 with TGA 24 hours before and 48 hours after CPB. In addition to cerebral oxygen saturation, routine measurements of oxygen transport and delivery were performed.

Results: Preoperatively, cerebral oxygen saturation was higher in patients with HLHS than with TGA (61% ± 7% vs 56% ± 8%, $P = .04$). After CPB, cerebral oxygen saturation was markedly depressed in both groups but increased toward end of monitoring (HLHS vs TGA minimal value 42% ± 12% vs 54% ± 11%, $P < .001$, value 48 hours after CPB 62% ± 7% vs 80% ± 8%, $P < .0001$). Routine measures of oxygen delivery, such as arterial and central venous oxygen saturations, were similar at minimal cerebral oxygen saturation and 48 hours after CPB.

Conclusions: Depression of cerebral oxygen saturation is prevalent among neonates with congenital heart disease regardless of whether univentricular or biventricular circulation is present, suggesting that cerebral desaturation is mainly induced by CPB's effect on cerebral blood flow. Routine measures of oxygen delivery fail to indicate cerebral desaturation. (J Thorac Cardiovasc Surg 2011;142:523-30)

Complex cyanotic congenital heart defects such as hypoplastic left heart syndrome (HLHS) and transposition of the great arteries (TGA) necessitate neonatal surgical intervention. The Norwood procedure and its modifications are used as initial palliation for HLHS, and the arterial switch operation (ASO) is used to correct TGA. Both interventions these days are being performed with decreasing morbidity and mortality.[1,2] Despite this improvement, postoperative hemodynamic instability and potential adverse effects of hypothermic cardiopulmonary bypass (CPB) on oxygen delivery are suggested to be associated with adverse outcome and long-term neurologic dysfunction.[3]

Near-infrared spectroscopy (NIRS) provides a noninvasive means of evaluating regional cerebral oxygen saturation (Sco_2) and somatic oxygen saturation (Sso_2).[4] Previous studies have demonstrated that Sco_2, although maintained as much as possible during CPB with deep hypothermia and selective antegrade cerebral perfusion, is significantly depressed relative to Sso_2 in the early post-CPB period after the Norwood procedure in patients with HLHS, suggesting that cerebrovascular resistance is increased after deep hypothermic CPB.[5] Hemodynamic instability after the Norwood operation, with excessive pulmonary blood flow through a modified Blalock–Taussig shunt (MBTS) and significant diastolic runoff from the cerebral vascular bed, has also been discussed as possibly contributing to this phenomenon.[3]

We decided to monitor continuously regional oxygen saturation in patients with HLHS before and after the Norwood operation and also in neonates with TGA before and after the ASO to elucidate further whether postoperative changes in regional tissue oxygenation are related to inherent effects of deep hypothermic CPB or to hemodynamic alterations related to the single-ventricle physiology.

MATERIALS AND METHODS

Patients

Thirty-three consecutive patients with HLHS undergoing the modified Norwood operation and another 20 consecutive patients with TGA undergoing the ASO were enrolled in the study. All patients underwent surgery in the period from September 2006 to December 2008. All parents gave their

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Abbreviations and Acronyms

Ω	= oxygen excess factor
ASO	= arterial switch operation
$avDo_2$	= arteriovenous oxygen content difference
CPB	= cardiopulmonary bypass
HLHS	= hypoplastic left heart syndrome
MBTS	= modified Blalock–Taussig shunt
NIRS	= near-infrared spectroscopy
PCICU	= pediatric cardiac intensive care unit
Sao_2	= arterial oxygen saturation
Sco_2	= cerebral oxygen saturation
Sso_2	= somatic oxygen saturation
Svo_2	= central venous oxygen saturation
TGA	= transposition of the great arteries

informed consent to the collection and anonymous analysis of the data, and the study protocol was approved by the local research ethics committee.

Preoperative Management

Preoperatively, all patients with HLHS were treated according to a standardized protocol, as previously described,[1] consisting of afterload reduction with sodium nitroprusside or phentolamine mesylate (INN phentolamine mesilate), low-dose prostaglandin E_1, furosemide, enteral feeding, and avoidance of mechanical ventilation or inotropic support.

Of the 20 patients with TGA, 9 (45%) required a balloon atrioseptostomy on the day of birth, and 2 patients transiently required mechanical ventilation. No additional preoperative medical treatment was necessary in this patient group.

Surgical Techniques

Patients with HLHS underwent the Norwood procedure with MBTS placement (3.0 or 3.5 mm). All patients with HLHS were operated on with low-flow antegrade selective cerebral perfusion during reconstruction of the aortic arch so that deep hypothermic circulatory arrest could be avoided. Only a single patient with an absent truncus brachiocephalicus received a 4-mm right ventricle–pulmonary artery conduit and needed a 7-minute period of deep hypothermic circulatory arrest.

The technique used for the ASO has previously been reported.[6] The Lecompte maneuver was used in all cases. Associated procedures included closure of a ventricular septal defect in 2 cases.

In both the HLHS and the TGA groups, the pH-stat method was used for cooling to a temperature of 18°C and was continued during CPB. The patients were rewarmed with the α-stat method. In all cases, hemofiltration was routinely used before weaning from CPB. In all patients, general anesthesia was maintained with inhaled sevoflurane, intravenous sufentanil, and rocuronium bromide.

Postoperative Management

Postoperatively, patients with HLHS were continued on afterload reduction therapy with either sodium nitroprusside or phentolamine mesylate, and inotropic support was achieved with epinephrine and enoximone.[1] For patients with TGA, a similar postoperative drug regimen was applied. The type of afterload reduction was determined clinically, with analysis of the effect of different types of afterload reduction on the postoperative course initially not intended. For patients with HLHS who had cyanosis, we aimed for a postoperative hemoglobin level of about 14 to 16 g/dL, corresponding with a hematocrit greater than 40%. For patients with TGA, we aimed for a hemoglobin level in the range of 12 to 14 g/dL, corresponding with a hematocrit of at least 30%.

Perioperative Monitoring and Data Acquisition

In all patients, both those with HLHS and those with TGA, invasive arterial blood pressure monitoring was initiated after admission to the pediatric cardiac intensive care unit (PCICU). Arterial oxygen saturation (Sao_2) was also continuously monitored. Immediately before surgery, a central venous line was placed in the superior vena cava, and each patient was intubated and mechanically ventilated.

Postoperative monitoring in the PCICU consisted of the continuous measurement of invasive arterial blood pressure, central venous blood pressure, Sao_2, and end-tidal Pco_2. Arterial blood gas values were checked hourly for the first 24 hours and thereafter at 2- to 4-hour intervals, depending on the patient status. Central venous blood gas values were analyzed at 4-hour intervals for the first 48 postoperative hours, starting after hemodynamic stabilization after arrival in the PCICU and afterward at clinically appropriate intervals. Blood gas tensions were reported at 37°C (Radiometer ABL, Copenhagen, Denmark). For hemodynamic monitoring, the IntelliVue system (Philips Healthcare, Best, The Netherlands) was used. All hemodynamic and blood gas data were recorded in the patients PCICU charts. Continuous measurements were recorded hourly. All hemodynamic and respiratory data were manually transferred in hourly intervals into a custom-made data base.

For the continuous recording of regional oxygen saturation, NIRS probes were placed on the patient's midline forehead (Sco_2) and slightly to the right of midline on the T10 to L2 posterior flank (Sso_2). The probes were monitored by a dual detector device (Somanetics INVOS 5100C; Somanetics Corporation, Troy, Mich). Cerebral and somatic NIRS data were stored digitally with a sampling rate of 1 per second and transferred into a commercial spreadsheet application. Thereafter, all values recorded in an hour were averaged and imported into the custom-made database system so that they could be matched with the hemodynamic and respiratory data of the respective time points.

Hemodynamic, respiratory, and NIRS data were collected and analyzed for the 24-hour interval before CPB and the 48-hour period after CPB.

Analysis and Calculations

Demographic and operative patient data were collected at the time of analysis from the patient records (Table 1). The durations of CPB, aortic crossclamping, and deep hypothermic circulatory arrest were also recorded, as were the duration of ventilation, circulatory drug support, and duration of PCICU treatment.

To quantify differences between Sco_2 and Sso_2 between patients with HLHS and those with TGA, the following parameters were calculated (Figure 1): (1) average Sco_2 and Sso_2 calculated for the first 10 preoperative hours, (2) minimal postoperative Sco_2, (3) interval from the end of CPB to the minimal Sco_2, (4) Sco_2 and Sso_2 at the end of registration (48 hours after CPB), and (5) interval needed to increase Sco_2 to halfway toward the late postoperative level.

To delineate any potential differences in blood pressure and routine postoperative measurements of oxygen delivery at the times of minimal and maximal postoperative Sco_2, central venous and arterial blood pressures, Sao_2, central venous oxygen saturation sampled from the central venous catheter placed in the superior vena cava (Svo_2), arteriovenous oxygen content difference ($avDo_2$), oxygen excess factor (Ω), and hemoglobin concentration were all compared at both time points in both groups. The Ω value is regarded as a valid measure of systemic oxygen delivery and is calculated as the ratio of Sao_2 to the difference between Sao_2 and Svo_2.[7]

Low values for Svo_2 have also been shown to indicate impaired systemic oxygen delivery.[7] We therefore compared postoperative Svo_2 values with regional tissue oxygenation measured by NIRS (Sco_2 and Sso_2).

TABLE 1. Demographic and surgical patient data

	HLHS (n = 33)	TGA (n = 20)	*P* value
Male (No.)	20 (61%)	16 (80%)	NS
Birth weight (kg, mean ± SD)	3.3 ± 0.5	3.5 ± 0.6	NS
Age at surgery (d, mean ± SD)	6.4 ± 4.4	7.1 ± 3.1	NS
Weight at surgery (kg, mean ± SD)	3.2 ± 0.5	3.5 ± 0.6	NS
BSA at surgery (m^2, mean ± SD)	0.21 ± 0.02	0.22 ± 0.02	NS
Duration of CPB (min, mean ± SD)	144 ± 22	151 ± 22	NS
Duration of aortic crossclamping (min, mean ± SD)	44 ± 14	88 ± 19	<.0001
Duration of DHCA (min, mean ± SD)	0 (0–7)	0 (0–8)	NS
Early (30-d) survival (No.)	33 (100%)	20 (100%)	NS
Postoperative ventilation (h, mean ± SD)	58 (36–192)	50 (15–133)	.07
Postoperative PCICU stay (h, mean ± SD)	88 (50-696)	72 (43-133)	.08
Duration of epinephrine use (h, mean ± SD)	42 (22-575)	27 (16-104)	.10
Duration of sodium nitroprusside use h,* mean ± SD)	51 (3-125)	31 (13-88)	NS
Duration of phentolamine mesylate use (h,* mean ± SD)	71 (27-696)	71 (31-96)	NS
Duration of enoximone use (h, mean ± SD)	82 (29-696)	71 (42-128)	.05

HLHS, Hypoplastic left heart syndrome; *TGA,* transposition of the great arteries; *NS,* not significant; *BSA,* body surface area; *CPB,* cardiopulmonary bypass, *DHCA,* deep hypothermic circulatory arrest; *PCICU,* pediatric cardiac intensive care unit. *Sodium nitroprusside was used in 14 patients with hypoplastic left heart syndrome and in all patients with transposition of the great arteries; phentolamine mesylate was used in 19 patients with hypoplastic left heart syndrome and in 5 patients with transposition of the great arteries.

Low Sco_2 after CPB has been suggested to be related to low $Paco_2$.[5] The relationship between Sco_2 and $Paco_2$ was therefore calculated at the time of minimal Sco_2 for both groups, patients with HLHS and those with TGA.

To detect any impact of low Sco_2 after CPB on adverse outcome, we divided the HLHS and TGA groups according to the median duration of PCICU treatment. The end of PCICU treatment was defined as the point at which mechanical ventilation and circulatory drug support were ultimately terminated. Thereafter we compared post-CPB Sco_2 values in patients with durations of PCICU treatment longer and shorter than the median with a general linear model repeated-measures analysis of variance.

Regional tissue oxygenation was also compared between patients with HLHS who received sodium nitroprusside to reduce systemic afterload after the Norwood operation and those who received phentolamine mesylate.

Statistics

Data are presented as mean ± SD or median and range as appropriate. Comparisons between groups and variables were made with the Student *t* test or Mann–Whitney *U* test, and paired analyses were performed with the Student *t* test or Wilcoxon signed rank test as appropriate. Univariate linear regression analyses were performed to assess associations between variables.

A general linear model repeated-measures analysis of variance was used to compare NIRS values between the subgroups of patients with durations of PCICU treatment longer and shorter than the median and between those who received sodium nitroprusside to reduce systemic afterload and those who received phentolamine mesylate.

All analyses were preformed with SPSS 17.0 for Windows software (SPSS Inc, an IBM Company, Chicago, Ill). For multiple comparisons of blood gas data and NIRS data in subsequent postoperative intervals, the level of significance was adjusted according to the number of comparisons made with the Bonferroni method.

RESULTS

Patient Characteristics and Surgical Data

Demographic and surgical patient data are summarized in Table 1. Patients with HLHS and patients with TGA did not differ with regard to sex distribution, birth weight, age, weight, and body surface area at surgery. CPB times and deep hypothermic circulatory arrest times were also similar in the 2 groups. Patients with TGA had a significantly longer aortic crossclamp time. There were nonsignificant trends toward longer ventilation time and longer PCICU treatment in patients with HLHS ($P = .07$ and $P = .08$, respectively). Durations of epinephrine and enoximone support also tended to be longer in the HLHS group ($P = .10$ and $P = .05$, respectively).

None of the patients with HLHS and patients with TGA died within 30 days after the operation. All patients with HLHS survived until the subsequent hemi-Fontan operation.

Preoperative and Postoperative Profiles of Regional Tissue Oxygenation

Figure 1 shows the data for regional oxygen saturation as recorded for 24 hours before and 48 hours after CPB in both patients with HLHS and patients with TGA. In the 10 hour period before CPB, mean Sco_2 was significantly higher in patients with HLHS than in patients with TGA (61% ± 7% vs. 56% ± 8%, $P = .04$). Sso_2 did not differ between patients with HLHS and patients with TGA when comparing the mean values of the first 10 hours of preoperative monitoring (60% ± 8% vs. 61% ± 8%, *P* not significant).

After cessation of CPB, there was a marked decrease in Sco_2 in both groups of patients with congenital heart disease. The minimal Sco_2 was recorded after 5.1 ± 1.6 hours in patients with HLHS and after 4.7 ± 2 hours in patients with TGA (*P* not significant). In patients with HLHS, Sco_2 fell after CPB to a minimum of 42% ± 12%, whereas in patients with TGA it fell to 54% ± 11% ($P < .001$). Thereafter, Sco_2 continuously increased and reached a plateau approximately 24 hours after weaning from CPB, with Sco_2 values in the range of the 48-hour level. After 48 hours, Sco_2 was 62% ± 7% in patients with HLHS and 80% ± 8% in patients with TGA ($P < .0001$). In patients with HLHS, it took 5.5 ± 4.7 hours to increase Sco_2 halfway toward the 48-hour level. In patients with TGA, the necessary interval was in the same range (4.1 ± 3.3 hours, *P* not significant).

Compared with Sco_2, Sso_2 showed less marked changes during postoperative monitoring. In patients with TGA

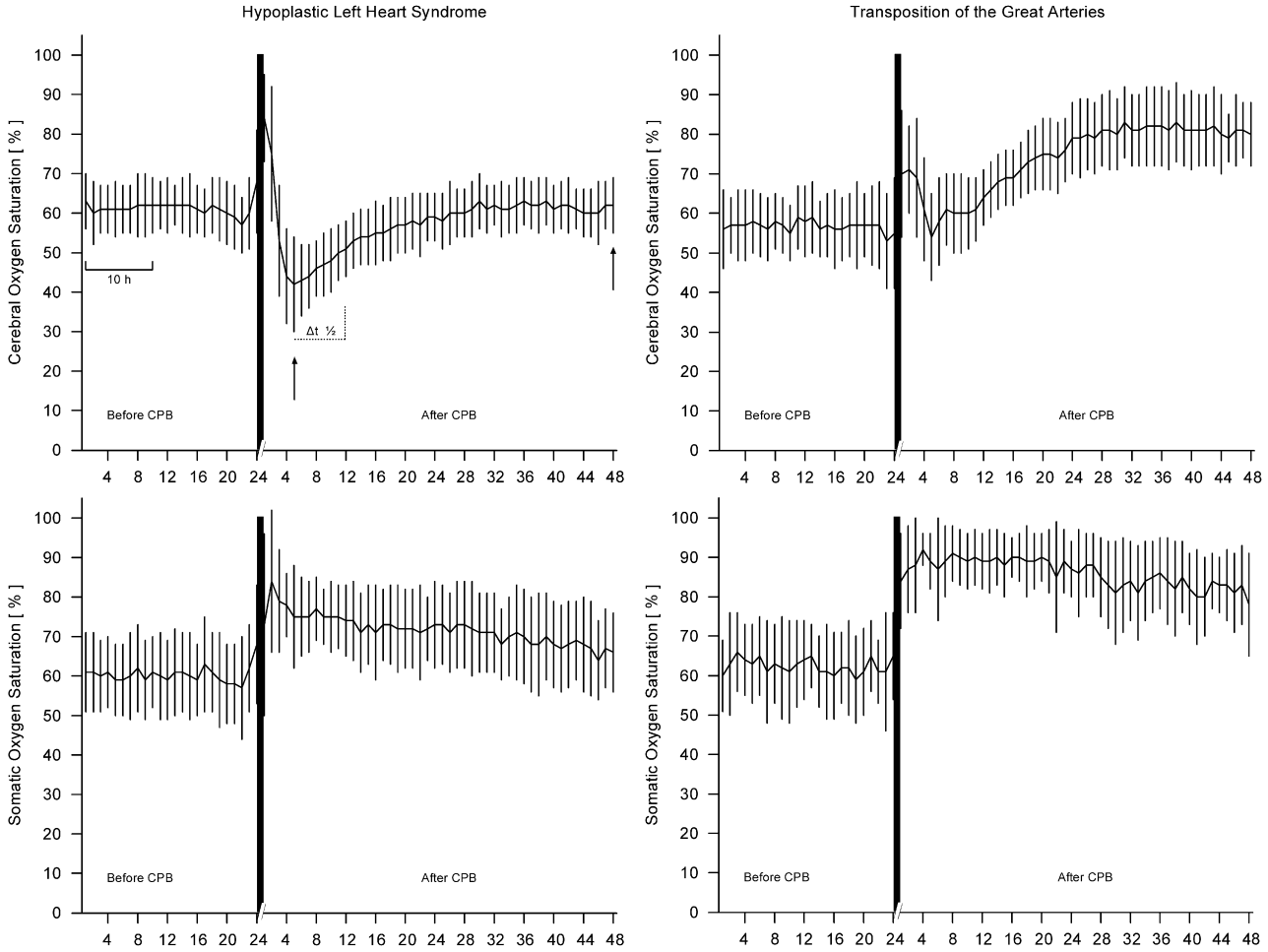

FIGURE 1. Perioperative profiles of regional tissue oxygenation. The *black vertical bar* indicates the cardiopulmonary bypass *(CPB)* period. In the *left upper panel,* the 10-hour period taken to compare near-infrared spectrographic data before cardiopulmonary bypass is marked. The time points of minimal cerebral oxygen saturation and late postoperative cerebral oxygen saturation are marked with an *arrow. Δ½,* Time to increase cerebral oxygen saturation halfway toward its 48-hour value.

without cyanosis, Sso_2 was higher both early and late after CPB. The difference in postoperative Sso_2 between patients with TGA and patients with HLHS is exemplified by the statistical difference between the postoperative peak and 48-hour values (TGA vs HLHS peak Sso_2 92% ± 4% vs 84% ± 15%, 48-hour Sso_2 78% ± 13% vs 66% ± 10%, $P < .05$ and $P < .0001$, respectively). In both groups, Sso_2 decreased mildly from the early postoperative peak to the level of the 48-hour value.

Sco_2, Blood Pressure, and Conventional Hemodynamic Measurements

The changes in postoperative Sco_2 were most pronounced in the early postoperative period. To assess whether the depression in Sco_2 early after CPB and the subsequent recovery were accompanied by changes in blood pressure and parameters related to oxygen transport and delivery, central venous pressure, mean arterial blood pressure, hemoglobin levels, Sao_2, Svo_2, $avDo_2$, and Ω were measured at the times of minimal and maximal postoperative Sco_2, and these values were compared. These data are given in Table 2. In patients with HLHS, mean arterial blood pressure was higher at the time of minimal Sco_2. Other than this, none of the parameters changed significantly from the time of minimal Sco_2 to that of maximal Sco_2. In patients with TGA, only $avDo_2$ and Ω indicated an improvement oxygen delivery; however, Sao_2 and Svo_2 also failed to indicate impaired cerebral tissue oxygenation.

Postoperative Regional Oxygenation Saturations, Sao_2, and Svo_2

Figure 2 shows the data for postoperative regional oxygen saturations in conjunction with the simultaneous measurements of Sao_2 and Svo_2, as obtained from blood gas analysis, for both groups of patients with congenital heart disease. As mentioned previously, blood gas data

TABLE 2. Blood pressures and measurements related to oxygen transport and delivery at minimal and maximal postoperative cerebral tissue oxygenations

	HLHS			TGA		
	Sco_2min	Sco_2max	*P* value	Sco_2min	Sco_2max	*P* value
CVP (mm Hg)	7.8 ± 2.3	8.8 ± 2.6	NS	7.2 ± 1.9	8.7 ± 2.1	NS
Mean ABP (mm Hg)	60.0 ± 8.1	53.6 ± 7.9	.003	61.1 ± 11.5	57.3 ± 10.0	NS
Hemoglobin (g/dL)	14.1 ± 1.0	14.2 ± 1.0	NS	13.6 ± 1.9	12.6 ± 1.6	.07
Sao_2 (%)	80.0 ± 5.7	81.0 ± 4.8	NS	99.0 ± 1.3	99.0 ± 0.8	NS
Svo_2 (%)	62.2 ± 9.0	63.3 ± 9.0	NS	71.7 ± 8.8	76.9 ± 6.3	.07
$avDo_2$ (mL/dL)	3.0 ± 1.4	3.5 ± 1.3	NS	6.1 ± 2.8	3.4 ± 1.3	<.001
Ω	5.3 ± 1.9	5.4 ± 2.2	NS	3.0 ± 0.9	5.0 ± 2.0	<.001

All values are mean ± SD. *HLHS,* Hypoplastic left heart syndrome; *TGA,* transposition of the great arteries; *Sco_2min,* minimal cerebral tissue oxygenation; *Sco_2max,* maximal cerebral tissue oxygenation; *CVP,* central venous pressure; *NS,* not significant; *ABP,* arterial blood pressure, *Sao_2,* arterial oxygen saturation; *Svo_2,* venous oxygen saturation; *$avDo_2$,* arteriovenous oxygen content difference; *Ω,* oxygen excess factor ($Sao_2/[Sao_2 - Svo_2]$).

could not be collected hourly, so comparisons between blood gas data and data on regional tissue oxygenation had to be made after calculation of mean values for consecutive 4-hour intervals. These mean values were compared to delineate potential differences between blood gas and NIRS data. This analysis showed that in patients with HLHS, Svo_2 was significantly higher than Sco_2 at 4 to 8, 8 to 12, 12 to 16, and 16 to 20 hours after surgery ($P < .005$ for each interval). In patients with TGA, comparable differences could be found. In the latter group, the difference between Svo_2 and Sco_2 was significant at 4 to 8, 8 to 12, and 12 to 16 hours after surgery ($P < .005$ for each interval). Compared with Sso_2, Svo_2 was lower during the early postoperative period both in patients with HLHS and in patients with TGA. In patients with HLHS, the difference in Svo_2 and Sso_2 was significant at 4 to 8, 8 to 12, 12 to 16, and 16 to 20 hours ($P < .001$ for each interval). In patients with TGA, the difference remained significant until the interval from 32 to 36 hours after cessation of CPB ($P < .001$ for each interval). Sao_2 remained unchanged during the entire period of postoperative monitoring and was unrelated to the changes in regional tissue oxygenation (Figure 2).

Sco_2 and Adverse Outcome

Adverse outcome was defined as duration of PCICU treatment longer than the median of the respective group (Table 1). In both patients with HLHS and patients with TGA, there was no difference in postoperative Sco_2 between the subgroups of patients with adverse outcome and those without when comparing the Sco_2 curves for the respective subgroups with repeated-measures analysis of variance (Figure 3). There was also no relationship between Sso_2 and adverse outcome in either group.

Correlates With Low Postoperative Sco_2

We found a significant correlation between Sco_2 and the corresponding Pco_2 in patients with HLHS at time of minimal Sco_2 ($r = 0.49$, $P < .01$). We could not, however, demonstrate such a relationship for the groups of patients with TGA ($r = –0.05$, *P* not significant).

In the HLHS groups, 14 patients received sodium nitroprusside to reduce afterload and 19 patients received phentolamine mesylate, so the Sco_2 curves for these 2 HLHS subgroups were compared with repeated-measures analysis of variance. The type of afterload reduction did not affect the postoperative course of Sco_2 in patients with HLHS.

DISCUSSION

The major finding of this study was that Sco_2 decreased significantly after CPB in neonates undergoing surgery for complex congenital heart disease. A dip in Sco_2 was found both in patients with HLHS who had cyanosis after the Norwood operation and in patients with TGA who did not have cyanosis after the ASO. We therefore presume that the postoperative depression in Sco_2 is most likely related to a direct effect of hypothermic CPB rather than to the presence or absence of a parallel circulation.

We studied patients with HLHS and TGA. Because the patient groups were similar with regard to age at operation, duration of CPB, and the type of postoperative medical treatment, they seemed particularly suitable for a study aiming to delineate any differences in the course and level of regional tissue oxygenation potentially related to the presence or absence of cyanosis or the type of circulation.

The decrease in Sco_2 immediately after CPB has previously been reported to be almost universally present in patients with HLHS after the Norwood operation.[3,5,8] It has been speculated by Hoffmann and coworkers[5] that this depression is related to a transient increase in cerebrovascular resistance. Phelps and coworkers,[3] however, showed that the postoperative decrease in Sco_2 tended to be less pronounced in patients with HLHS who had right ventricular to pulmonary artery conduit (Sano shunt) placement relative to those who had MBTS placement. They therefore speculated that an abnormal cerebral blood flow caused by the proximity of the MBTS to the cerebral arteries also contributes to this phenomenon. Except in 1 case, all patients with HLHS studied by us were operated on with MBTS placement. We therefore can not contribute to the

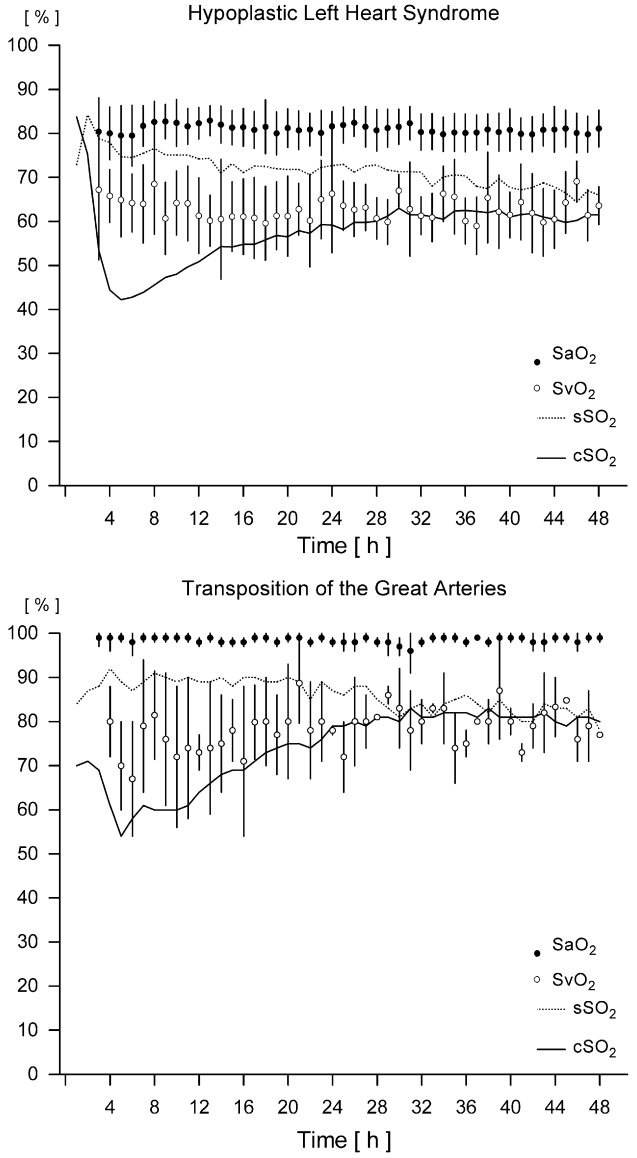

FIGURE 2. Postoperative regional tissue oxygenations, arterial oxygen saturation *(SaO_2),* and central venous oxygen saturation *(SvO_2). sSO_2,* Somatic oxygen saturation, *cSO_2,* cerebral oxygen saturation.

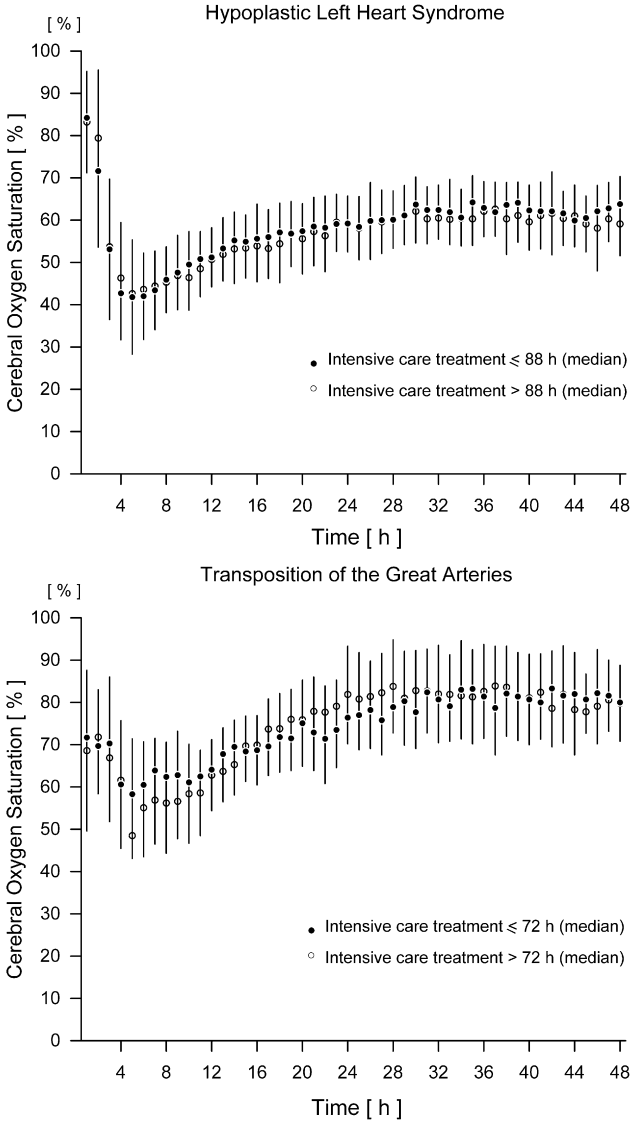

FIGURE 3. Postoperative cerebral oxygen saturation separated into good outcomes and adverse outcomes (duration of intensive care treatment longer than the median of the respective group).

determination of whether MBTS placement particularly impairs Sco_2 in patients with HLHS. The fact that patients with TGA showed a similar decrease in Sco_2, albeit without cyanosis after surgery on a higher level, strongly suggests that cerebrovascular autoregulation is significantly disturbed after CPB and that this disturbance is the predominant contributor to abnormal early postoperative cerebral oxygen delivery.

In our cohort of patients with HLHS early after neonatal surgery, we could not find any significant relationship between routine measures of oxygen transport and delivery such as hemoglobin concentration, Svo_2, $avDo_2$, or Ω (Figure 2 and Table 2). Svo_2 has been reported to be closely related to Sco_2 in older children with a univentricular circulation.[9] This discrepancy with our early postoperative data might be explained by the fact that postoperative Svo_2 measurement could be in error when sampling central venous blood from a central venous line placed in the superior vena cava in close proximity to pulmonary venous blood flow through an open interatrial communication. This might cause Svo_2 and thus $avDo_2$ to be overestimated by sampling a mixture of central venous and pulmonary venous blood. We could not, however, even demonstrate a trend toward higher Svo_2 or any difference in $avDo_2$ or Ω from the early post-CPB period toward the end of NIRS monitoring. Furthermore, the increase in Svo_2 from the time point of minimal Sco_2 to the time of maximal Svo_2 in patients with TGA was also not pronounced.

Li and colleagues[10] have also reported on a correlation between Sco_2 and Svo_2, collecting these data in 11 patients with HLHS during a period of 72 hours after the Norwood operation. In that prospective study, data were collected at 2-hour intervals and only if sedation, paralysis, and ventilatory or hemodynamic treatments were not changed for 15 minutes before the sampling. In our study, NIRS data were collected continuously, and central venous blood was sampled 4-hourly, starting after stabilization of the patient after arrival on the PCICU and thereafter at different time points. Svo_2 data were therefore not available for all patients at all time points, but NIRS data were, and data may well have been collected at times of hemodynamic instability or change. Furthermore, even though a statistically significant relationship between Sco_2 and Svo_2 exists in postoperative patients with HLHS, the strength of this relationship does not seem strong enough to predict with accuracy a specific cerebral NIRS value from a given value of Svo_2. For example, Svo_2 of 60% did correspond with Sco_2 in the range 30% to 70% in the study of Li and colleagues.[10] We presume that the difference in data collection and the weakness of the relationship between Svo_2 and Sco_2 could explain why the marked and rapid changes in Sco_2 observed in our patients early after the Norwood operation were not mirrored by similar changes in Svo_2 or derived measures of oxygen transport and delivery. We suggest therefore that NIRS monitoring may be an important complementary tool in an attempt to monitor neonates comprehensively early after complex neonatal heart surgery.

We found significantly higher blood pressures at the time of lowest Sco_2 early after the Norwood operation (Table 2). This finding is compatible with a recent study by Lucas and coworkers,[11] which showed an inverse relationship between mean arterial blood pressure and Sco_2 measured by NIRS in healthy human subjects when altering blood pressure pharmacologically. Our finding, and likewise that of Lucas and coworkers,[11] may be explained by cerebral vasoconstriction or dilatation introduced by the pharmaceutical agents used. Postoperative changes in skin blood flow, however, could also explain these findings.[12]

NIRS measures the oxygen saturation of blood in the arterial, capillary, and venous vascular compartments. In the brain, the venous compartment has the highest capacitance. An elevated central venous pressure may therefore increase the volume of blood in the venous compartment more than those in the arterial and capillary compartments, potentially resulting in lower NIRS values. We could not detect any difference in central venous pressures, however, when comparing the time points of the lowest and highest postoperative NIRS Sco_2 values (Table 2). Changes in central venous pressure are therefore unlikely to explain the depression in Sco_2 early after neonatal surgery with CPB reported here.

Experimental data suggest that significant postoperative cerebral deoxygenation is likely to impact negatively on neurodevelopmental outcome in children undergoing neonatal surgery with CPB.[13,14] It therefore seems vital to detect any cerebral desaturation and to develop strategies to reduce the degree of desaturation. The decrease in Sco_2 is to some extent mirrored by a peak in Sso_2 and vice versa, with Sco_2 increasing with time and Sso_2 falling during the first 48 hours after CPB. The observation of this phenomenon has led to the development of the hypothesis that the depression in Sco_2 could be aggravated by redistribution of blood from the cerebral circulation toward the splanchnic circulation, because α-blocking vasodilative drugs such as phentolamine mesylate are more active in splanchnic, muscle, and skin vascular beds than in the brain, with its intense autoregulation.[5] This redistribution could potentially be aggravated by aggressive postoperative vasodilator therapy. Although we could not demonstrate any difference in the level and course of postoperative Sco_2 between our subgroups of patients with HLHS treated with sodium nitroprusside and with phentolamine mesylate, further prospective studies with vasodilative drugs that have been shown to increase cerebral blood flow after CPB, such as milrinone, are warranted and underway.[15]

Phelps and coworkers[3] showed that low Sco_2 measured by NIRS in the first 48 hours after the Norwood operation has a strong association with adverse outcome. In their study, adverse outcome was defined as PCICU stay longer than 30 days, need for extracorporeal membrane oxygenation, or in-hospital death after 48 hours. Because none of our patients died after either the Norwood operation or the ASO, we defined adverse outcome as duration of PCICU treatment longer than the median in the respective patient group, which was 88 hours for the Norwood operation and 72 hours for the ASO. According to this definition, we could not detect any difference in Sco_2 related to adverse outcome in either patients with HLHS or patients with TGA.

Hypocapnia has been shown to contribute to low postoperative Sco_2 in patients with HLHS undergoing the Norwood operation.[5] In our study we also demonstrated a relationship between Sco_2 and Pco_2 in patients with HLHS when calculating this relationship at the time of minimal Sco_2. No similar association, however, could be found in neonates after the ASO. The fact that Pco_2 relates to Sco_2 in patients with HLHS might indicate simply that alterations in pulmonary blood flow through the MBTS and associated alterations in pulmonary blood flow contribute to some extent to cerebral desaturation after CPB,[16] an effect that is not possible in patients with TGA because the pulmonary and systemic circulations are in series. Our data therefore suggest that early postoperative mechanical ventilation should aim to avoid any degree of hyperventilation in patients with a univentricular circulation and an aortopulmonary shunt. In our department, a postoperative arterial Pco_2 of about 45 mm Hg is the aim for this patient group.

Study Limitations

Isoflurane decreases cerebral oxygen consumption and cerebrovascular resistance, with a resultant increase in Sco_2.[17] The sudden cessation of isoflurane at the end the Norwood procedure may therefore also have contributed to postoperative cerebral desaturation. The design of this study does not allow us to distinguish between the effects of general anesthesia on Sco_2 and those of CPB.

Svo_2 was sampled from the central venous catheter placed in the superior vena cava. The Svo_2 values reported here thus do not truly represent mixed venous oxygen saturation but rather venous blood flow from the brain, head, and upper extremities.

Cerebral NIRS values predominantly represent brain oxygenation but also that of adjacent and overlying tissues. A good and close correlation between cerebral NIRS values and sagittal sinus blood oxygenation has recently been demonstrated, however, in an animal study on newborn piglets.[18]

CONCLUSIONS

In conclusion, a depression of Sco_2 as measured by NIRS is prevalent among neonates with complex congenital heart disease early after cessation of CPB. A dip in Sco_2 was found both in patients with HLHS who had cyanosis after the Norwood operation and in patients with TGA who did not have cyanosis after the ASO. This result indicates that early postoperative cerebral desaturation is potentially induced by a direct effect of CPB on cerebral blood flow rather than by the presence of a univentricular circulation. Further prospective studies are warranted to develop treatment strategies to reduce the degree of cerebral desaturation.

Because routine measures of oxygen transport and delivery do not clearly indicate any cerebral desaturation, cerebral NIRS monitoring may be an important complementary tool in an attempt to comprehensively monitor neonates early after complex neonatal heart surgery. It seems essential in the development of postoperative treatment strategies that aim to prevent neurologic damage most likely resulting from cerebral desaturation.

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